

WHAT IS CLAIMED IS:

1. A method of repairing injured genitourinary tract tissue, comprising:
injecting muscle-derived cells into the injured genitourinary tract tissue; said
muscle-derived cells genetically engineered to contain a heterologous gene
5 encoding a bioactive molecule functional in repair of the injured genitourinary
tissue, wherein the bioactive molecule is expressed by the injected muscle-derived
cells, resulting in the production of the bioactive molecule in and around the injured
tissue, and further wherein the production of the bioactive molecule is sustained in
the injured tissue to enhance treatment and repair of genitourinary tract injury
10 and/or to improve or alleviate a genitourinary tract dysfunction.
2. The method according to claim 1, wherein the muscle-derived cells
are selected from the group consisting of myoblasts and muscle-derived stem cells.
3. The method according to claim 1, wherein the muscle-derived cells
are myoblasts and muscle-derived stem cells.
- 15 4. The method according to claim 1, wherein the muscle-derived cells
are autologous to a host being treated.
5. The method according to claim 1, wherein the bioactive molecule is
selected from the group consisting of protein, polypeptide, peptide, drug, enzyme,
hormone and metabolite.
- 20 6. The method according to claim 1, wherein the bioactive molecule is
inducible nitric oxide synthase (iNOS).
7. The method according to claim 1 wherein the genitourinary tract
dysfunction is selected from the group consisting of bladder inflammation, urinary
stress incontinence and erectile dysfunction.
- 25 8. The method according to claim 1, further comprising injecting the
same or different muscle-derived cells genetically engineered to contain a
heterologous gene encoding a trophic factor functional in the injured tissue,
wherein the trophic factor is produced by the injected muscle-derived cells in and

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around the injured tissue, and further wherein the production of the trophic factor is sustained in the injured tissue to ameliorate treatment of the genitourinary tract injury or dysfunction.

9. The method according to claim 8, wherein the trophic factor is a cytokine or growth factor.

10. The method according to claim 9, wherein the cytokine or growth factor is selected from the group consisting of acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, insulin-like growth factor, platelet derived growth factor, transforming growth factor- β , transforming growth factor- α , nerve growth factor and interleukin.

11. The method according to claim 1, wherein the muscle-derived cell is transduced with a viral vector containing the heterologous gene or transfected with plasmid DNA encoding a heterologous gene.

12. The method according to claim 11, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus, and retrovirus.

13. The method according to claim 1, further comprising injecting the same or different muscle-derived cell genetically engineered to contain a heterologous gene encoding an immune suppression factor functional in the injected tissue, wherein the immune suppression factor is produced by the injected muscle-derived cells in and around the injured tissue, and further wherein the production of the immune suppression factor is sustained in the injured tissue to allow survival of the injected cells and prevent an adverse immune response to the injected cells.

14. The method according to claim 13, wherein the immune suppression factor is interleukin-1 receptor agonist protein.

15. A method of repairing injured musculoskeletal tissue, comprising: injecting muscle-derived cells into injured musculoskeletal tissue; said muscle-

derived cells genetically engineered to contain a heterologous gene encoding a bioactive molecule functional in repair of the injured musculoskeletal tissue, said gene being expressed in the muscle-derived cells, resulting in the production of the bioactive molecule by the injected muscle-derived cells in the injured tissue, and further wherein the production of the bioactive molecule is sustained in the injured tissue to enhance treatment and repair of the musculoskeletal tissue.

16. The method according to claim 15, wherein the musculoskeletal tissue injury is associated with degenerative arthritis, cartilage damage, meniscus damage, ligament damage, joint damage, or rheumatoid disease.

17. The method according to claim 15, wherein the muscle-derived cells are transduced with a replication-defective viral vector or transfected with plasmid DNA containing the heterologous gene.

18. The method according to claim 15, wherein the muscle-derived cells are selected from the group consisting of myoblasts and muscle-derived stem cells.

19. The method according to claim 15, wherein the muscle-derived cells are myoblasts.

20. The method according to claim 15, wherein the muscle-derived cells are autologous to a host being treated.

21. The method according to claim 15, wherein the bioactive molecule is selected from the group consisting of protein, polypeptide, peptide, drug, enzyme, hormone and metabolite.

22. The method according to claim 15, further comprising injecting the same or different muscle-derived cells genetically engineered to contain a heterologous gene encoding a trophic factor functional in the injured tissue, wherein the trophic factor is produced by the injected muscle-derived cells in and around the injured tissue, and further wherein the production of the trophic factor is sustained in the injured tissue to enhance or ameliorate repair of the musculoskeletal tissue injury.

23. The method according to claim 22, wherein the trophic factor is a cytokine or growth factor.

24. The method according to claim 23, wherein the cytokine is selected from the group consisting of acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, insulin-like growth factor, platelet derived growth factor, transforming growth factor- β , transforming growth factor- α , nerve growth factor and interleukin, bone morphogenetic proteins, cartilage derived morphogenetic proteins, vascular endothelial growth factor and sonic hedgehog proteins.

25. The method according to claim 15, further comprising injecting the same or different muscle-derived cells genetically engineered to contain a heterologous gene encoding an immune suppression factor expressed by the muscle-derived cells and functional in the injected tissue, wherein the immune suppression factor is produced by the injected muscle-derived cells in and around the injured tissue, and further wherein the production of the immune suppression factor is sustained in the injured tissue to allow survival of the injected cells and prevent an adverse immune response to the injected cells.

26. The method according to claim 25, wherein the immunosuppression factor is interleukin-1 receptor agonist protein.

27. A method of repairing a bone defect, said bone defect associated with bone loss, bone deficiency, or bone weakness, comprising:

injecting muscle-derived cells into tissue surrounding the bone defect; said muscle-derived cells genetically engineered to contain a heterologous gene encoding a bioactive molecule functional in repair of the bone defect, wherein the bioactive molecule is produced by the injected muscle-derived cells and wherein the production of the bioactive molecule is sustained in the injured tissue to enhance or improve repair of the bone defect.

28. The method according to claim 27, wherein the bone defect is

selected from the group consisting of bone fracture, osteoporosis and osteosarcoma.

29. The method according to claim 27, wherein the muscle-derived cells are transduced with a replication-defective viral vector containing the heterologous gene.

30. The method according to claim 27, wherein the muscle-derived cells are transfected with DNA containing the heterologous gene.

31. The method according to claim 29, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus and retrovirus.

32. The method according to claim 27, wherein the muscle-derived cells are selected from the group consisting of myoblasts and muscle-derived stem cells.

33. The method according to claim 27, wherein the muscle-derived cells are myoblasts.

34. The method according to claim 27, wherein the muscle-derived cells are autologous to a host being treated.

35. The method according to claim 27, wherein the bioactive molecule is selected from the group consisting of protein, polypeptide, peptide, drug, enzyme, hormone and metabolite.

36. The method according to claim 35, wherein the bioactive molecule is osteogenic protein.

37. The method according to claim 36, wherein the osteogenic protein is bone morphogenic protein-2.

38. The method according to claim 27, further comprising injecting the same or different muscle-derived cells genetically engineered to contain a heterologous gene encoding a trophic factor functional in the injured tissue, wherein the trophic factor expressed the injected muscle-derived cells resulting in the production of the trophic factor in and around the injured tissue, and further

wherein the production of the trophic factor is sustained in the injured tissue to enhance or ameliorate repair of the bone defect.

39. The method according to claim 38, wherein the trophic factor is a cytokine or growth factor.

40. The method according to claim 39, wherein the cytokine is selected from the group consisting of acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, insulin-like growth factor, platelet derived growth factor, transforming growth factor- β , transforming growth factor- α , nerve growth factor and interleukin, bone morphogenetic proteins, cartilage derived morphogenetic proteins, vascular endothelial growth factor and sonic hedgehog proteins.

41. The method according to claim 27, further comprising injecting the same or different muscle-derived cells genetically engineered to contain a heterologous gene encoding an immune suppression factor functional in the injected tissue, wherein the immune suppression factor is expressed by the muscle-derived cells, resulting in the production of the immune suppression factor in and around the injured tissue, and further wherein the production of the immune suppression factor is sustained in the injured tissue to allow survival of the injected cells and prevent an adverse immune response to the injected cells.

42. The method according to claim 41, wherein the immunosuppression factor is interleukin-1 receptor agonist protein.

43. A method of treating a genitourinary tract dysfunction selected from the group consisting of bladder dysfunction and urinary stress incontinence, comprising:

injecting muscle-derived cells into injured bladder wall tissue; said muscle-derived cells being transformed with a vector containing a heterologous gene encoding human inducible nitric oxide synthase, wherein the inducible nitric oxide synthase is expressed by the transformed muscle-derived cells, thereby

resulting in increased production and release of nitric oxide by the injected muscle-derived cells into the injured bladder wall tissue to modulate muscle contractility in the bladder wall.

44. The method according to claim 43, wherein the muscle-derived cells are selected from the group consisting of myoblasts, myotube cells, muscle fiber cells, skeletal muscle cells and satellite cells.

45. The method according to claim 43, wherein the muscle-derived cells are myoblasts.

46. The method according to claim 43, wherein the muscle-derived cells are autologous to a host being treated.

47. The method according to claim 43, wherein the muscle-derived cells are transduced with a replication-defective viral vector containing the heterologous gene.

48. The method according to claim 47, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus and retrovirus.

49. A method of treating erectile dysfunction, comprising:
injecting muscle-derived into the corpora cavernosum of a male host; said muscle-derived cells being transformed with a vector containing a heterologous gene encoding human inducible nitric oxide synthase, wherein the inducible nitric oxide synthase is expressed by the transformed muscle-derived cells, thereby resulting in increased production and release of nitric oxide by the injected muscle-derived cells into the penile corpora, resulting in an increase in intracorporal pressure and penile erection therein.

50. The method according to claim 49, wherein the muscle-derived cells are selected from the group consisting of myoblasts which differentiate into myotube and muscle fiber as well as muscle-derived stem cells which can differentiate into muscle and other lineages.

51. The method according to claim 49, wherein the muscle-derived cells are myoblasts.

52. The method according to claim 49, wherein the muscle-derived cells are autologous to a host being treated.

5 53. The method according to claim 49, wherein the muscle-derived cells are transduced with a replication-defective viral vector containing the heterologous gene.

10 54. The method according to claim 53, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus and retrovirus.

55. The method according to claim 49 wherein the muscle-derived cells are transfected with plasmid DNA containing the heterologous gene.

56. A method of treating a muscle-related injury or dysfunction, or a bone-related injury or defect, comprising:

15 a) isolating muscle-derived cells from host muscle tissue;
b) culturing the muscle-derived cells under conditions allowing for proliferation of the cells;

20 c) transforming the cultured cells with a heterologous gene encoding a bioactive protein or functional portion thereof, said gene being expressed in the muscle-derived cells following injection of the cells into a site of muscle or bone injury in the host; and

25 d) injecting the transformed cells into a site near the muscle or bone in the host, thereby allowing the injected cells to express and produce the bioactive protein for treating the muscle-related injury or dysfunction, or the bone-related injury or defect.

57. The method according to claim 56, wherein the muscle-derived cells are selected from the group consisting of myoblasts and muscle-derived stem cells.

58. The method according to claim 56, wherein the muscle-derived cells

are myoblasts.

59. The method according to claim 56, wherein the muscle-derived cells are autologous to a host being treated.

60. The method according to claim 56, wherein the muscle-derived cells are transduced with a replication-defective viral vector containing the heterologous gene.

61. The method according to claim 60, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus and retrovirus.

62. The method according to claim 60, wherein the muscle-derived cells are transfected with plasmid DNA containing the heterologous gene.

63. Isolated genetically-engineered muscle-derived cells containing a heterologous gene encoding a inducible nitric oxide synthase, said nitric oxide synthase being expressed by the muscle-derived cells following injection of the cells into a site of injury selected from the group consisting of musculoskeletal tissue, bone and genitourinary tissue.

64. The cells according to claim 63, wherein the muscle-derived cells are selected from the group consisting of myoblasts and muscle-derived stem cells.

65. The cells according to claim 64, wherein the muscle-derived cells are myoblasts.

66. The cells according to claim 63, wherein the muscle-derived cells are autologous.

67. The cells according to claim 63, wherein the muscle-derived cells are genetically engineered with a replication-defective viral vector containing the inducible nitric oxide synthase gene.

68. The cells according to claim 67, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus and retrovirus.

69. Isolated genetically-engineered muscle-derived cells containing a heterologous gene encoding an osteogenic protein, said osteogenic protein being expressed by the muscle-derived cells following injection of the cells into a site of injury in bone, wherein the expressed osteogenic protein stimulates the muscle-derived cells to differentiate into bone cells.

70. The cells according to claim 69, wherein the muscle-derived cells are selected from the group consisting of myoblasts and muscle-derived stem cells.

71. The cells according to claim 69, wherein the muscle-derived cells are pre-osteoblast cells.

72. The cells according to claim 69, wherein the muscle-derived cells are autologous.

73. The cells according to claim 69, wherein the muscle-derived cells are genetically engineered with a replication-defective viral vector containing the inducible nitric oxide synthase gene.

74. The method according to claim 73, wherein the viral vector is selected from the group consisting of adenovirus, herpes simplex virus, adeno-associated virus, and retrovirus.

75. The cells according to claim 69, wherein the muscle-derived cells are transfected with plasmid DNA containing the inducible nitric oxide synthase gene.

76. A method of isolating and purifying muscle-derived stem cells, comprising:

- a) plating dissociated muscle cells on a collagen-coated substrate;
- b) isolating muscle-derived cell populations which adhere to said substrate at successive time intervals following said plating step a); and
- c) determining the characteristics of the isolated cell populations to identify muscle-derived stem cells.

77. The method according to claim 76, wherein the muscle cells are from

78. The method according to claim 76, wherein the the muscle-derived cell populations are isolated at one or more time intervals selected from the group consisting of one hour, two hours, eighteen hours, 24 hours, 48 hours, 72 hours, 96 hours and 120 hours after the plating step a).

79. The method according to claim 76, wherein, in step c), the characteristics determined are cell expression of one or more markers selected from the group consisting of desmin, BCL-2, CD34, myosin heavy chain isoforms, MyoD, myogenin and M-cadherin.

80. The method according to claim 79, wherein muscle-derived stem cells express high levels of desmin, BCL-2, CD34, myosin heavy chain isoforms; moderately high levels of MyoD and myogenin; and low levels of M-cadherin.

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